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=> s (IL-6 (a) receptor) (s) antibody (p) lymphocyte

L1 46 IL-6 (A) RECEPTOR (S) ANTIBODY (P) LYMPHOCYTE

=> dup rem l1

PROCESSING COMPLETED FOR L1
L2 20 DUP REM L1 (26 DUPLICATES REMOVED

=> s (IL-6 (a) receptor) (s) antibody (p) lymphocyte and human?

3 FILES SEARCHED...
L3 33 IL-6 (A) RECEPTOR (S) ANTIBODY (P) LYMPHOCYTE AND HUMAN?

=> dup rem l3

PROCESSING COMPLETED FOR L3
L4 16 DUP REM L3 (17 DUPLICATES REMOVED)

=> d l4 total ibib kwic

L4 ANSWER 1 OF 16 USPATFULL
ACCESSION NUMBER: 2000:117920 USPATFULL
TITLE: G-protein coupled receptor protein and a DNA encoding the receptor
INVENTOR(S): Hiruma, Shuji, Tsukuba, Japan
Hosoya, Masaki, Tsuchiura, Japan
Fujii, Ryo, Tsukuba, Japan
Ohtaki, Tetsuya, Tsukuba, Japan
Fukusumi, Shogi, Tsukuba, Japan
Ohgi, Kazuhiro, Tsukuba, Japan
PATENT ASSIGNEE(S): Takeda Chemical Industries, Ltd., Osaka, Japan
(non-U.S. corporation)

	NUMBER	DATE	
PATENT INFORMATION:	US 6114139	20000905	
	WO 9603502	19960222	
APPLICATION INFO.:	US 1995-513974	19950911	(8)
	WO 1995-JP1599	19950811	
		19950811	PCT 371 date
		19950811	PCT 102(e) date

	NUMBER	DATE
PRIORITY INFORMATION:	JP 1994-189272	19940811
	JP 1994-189273	19940811
	JP 1994-189274	19940811
	JP 1994-[illegible]56	19940830
	JP 1994-238757	19941003
	JP 1994-270027	19941102
	JP 1994-300621	19941202
	JP 1995-7177	19950120
	JP 1995-57186	19950316
	JP 1995-93889	19950419

DOCUMENT TYPE: Utility
PRIMARY EXAMINER: Walsh, Stephen
ASSISTANT EXAMINER: Park, Hankyel D.
LEGAL REPRESENTATIVE: Cushman, David G.; Resnick, David S.; Pike, Rosenstein, Kobert & Cushman, LLP
NUMBER OF CLAIMS: 6
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 10 Drawing Figure(s); 8 Drawing Page(s)
LINE COUNT: 1304
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L4 ANSWER 2 OF 16 USPATFULL
ACCESSION NUMBER: 2000:90586 USPATFULL
TITLE: Nucleic acid construct for expressing active substances which can be activated by proteases, and preparation and use
INVENTOR(S): Beidtmann, Hans Heinrich, Marburg, Germany, Federal Republic of
Mueller, Rolf, Marburg, Germany, Federal Republic of
Sedlacek, Hans-Harald, Marburg, Germany, Federal Republic of
PATENT ASSIGNEE(S): Hoechst Aktiengesellschaft AG, Germany, Federal Republic of (non-U.S. corporation)

	NUMBER	DATE	
PATENT INFORMATION:	US 6080575	20000627	
APPLICATION INFO.:	US 1998-8508	19980116	(9)

	NUMBER	DATE
PRIORITY INFORMATION:	DE 1997-19701141	19970116

DOCUMENT TYPE: Utility
PRIMARY EXAMINER: Kunz, Gary L.
ASSISTANT EXAMINER: Sun-Hoffman, Lin
LEGAL REPRESENTATIVE: Foley & Lardner
NUMBER OF CLAIMS: 22
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 5 Drawing Figure(s); 5 Drawing Page(s)
LINE COUNT: 2578
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
DETD Examples of promoters and activator sequences which are activated in **lymphocytes** and/or macrophages are the promoter and activator

sequences of the gene encoding cytokines, cytokine receptors and adhesion molecules, and receptors for the Fc fragment of **antibodies**. Examples of these are: IL-1 receptor, IL-1.alpha., IL-1.beta., IL-2, IL-2 receptor, IL-3, IL-3 receptor (.alpha. subunit), IL-3 receptor (.beta. subunit), IL-4, IL-4 receptor, IL-5, IL-6, **IL-6 receptor**, interferon regulatory factor 1 (IRF-1), [the promoter of IRF-1 is activated to the same extent by IL-6 as by IFN.gamma.]. . .

DETD . . . an antibody molecule or the epitope-binding moiety of an antibody molecule. The murine monoclonal antibodies should preferably be employed in **humanized** form. The **humanization** is effected in the manner described by Winter et al. Nature 349, 293 (1991) and Hoogenboom et al., Rev. Tr.. . .

DETD Recombinant antibody fragments are either prepared directly from existing hybridomas or are isolated from libraries of murine or **human** antibody fragments [Winter et al., Ann. Rev. Immun., 12, 433 (1994)] using the phage-display technique [Smith, Science 228, 1315 (1985)],. . .

DETD . . . also be used to isolate new antibody fragments directly from antibody libraries [immune libraries or naive libraries] of murine or **human** origin. In the phage-display of antibody fragments, the antigen-binding domains are cloned, as protein fusions with the coat protein pIII. . .

DETD . . . which are specific for murine [Orlandi et al., PNAS-U.S.A., 86, 3833 (1989), Sastry et al., PNAS-U.S.A., 86, 5728 (1989)] or **human** immunoglobulin genes [Barbas et al., BBRC 160, 1250 (1989)] or for the **human** immunoglobulin gene families [Marks et al., Eur. J. Immunol. 21, 985 (1991)].

DETD . . . revelation under stringent conditions [Hawkins et al., J. Mol. Biol. 226, 889 (1992)]. In addition, murine antibody fragments can be **humanized** by a stepwise replacement of one of the variable domains first by a **human** repertoire and then selecting with the original antigen (guided selection) [Jespers et al., Bio/Technol, 12, 899 (1994)]. Alternatively, murine antibodies are **humanized** by specifically replacing the hypervariable sections of **human** antibodies with the corresponding regions of the original murine antibody [Jones et al., Nature 321, 522 (1986)].

DETD . . . anchoring peptides include the transmembrane domains of cell membrane-located receptors or of viral proteins, such as the transmembrane sequence of **human** macrophage colony-stimulating factor (M-CSF; Ohashi et al., Oncogene 4, 1483 to 1490; Cosman et al., Behring Inst. Mitt. 83, 1 to 12 (1988)] or the DNA sequence for the signal and transmembrane regions of **human** respiratory syncytial virus (RSV) glycoprotein G [amino acids 1 to 63 or their part sequences, amino acids 38 to 63];. . .

DETD . . . Fc.mu. receptors of immune cells [Rojanasakul et al., Pharm. Res. 11, 171 (1994)]. They furthermore include the Fc fragment of **human** monoclonal or polyclonal immunoglobulin.

DETD . . . which activate the complement cascade, for example cobra venom factor [CVF or part sequences of CVF which correspond functionally to **human** complement factor C3b, i.e. which are able to bind to complement factor B and which, after having been cleaved by. . . for CVF and its part sequences were described by Fritzinger et al., Proc. Natl. Acad. Sci. U.S.A. 91, 12717 (1994)), **human** complement factor C3b (the DNA sequence for C3 and its part sequences were published by De Bruijn et al., Proc. Natl. Acad. Sci. U.S.A. 82, 708 (1985)), cleavage products of **human** complement factor C3 which resemble CVF functionally and structurally (such cleavage products have been described by O'Keefe et al., J.. . .

DETD . . . be a cytostatic, cytotoxic or inflammation-eliciting protein,

such as perforin, granzyme, cytokines, such as IL-1, IL-2, IL-4, IL-12, IL-3, IL-5, **human** leukemia inhibitory factor (LIF), IL-7, IL-11, IL-13, GM-CSF, G-CSFb or M-CSF, interferons, such as IFN.alpha., IFN.beta. or IFN.gamma., TNF, etc. . .

DETD . . . the active substance itself. Examples of such active compounds are bacterial nitroreductase, bacterial .beta.-glucuronidase, plant .beta.-glucuronidase derived from cereals, **human** .beta.-glucuronidase, **human** carboxypeptidase (CB), e.g. mast cell CB-A or pancreas CB-B, or bacterial carboxypeptidase, bacterial .beta.-lactamase, bacterial cytosine deaminase, **human** catalase or peroxidase, phosphatase, in particular **human** alkaline phosphatase or **human** acid prostate phosphatase, type 5 acid phosphatase, oxidase, in particular **human** lysyl oxidase or **human** acid D-aminooxidase, peroxidase, in particular **human** glutathione peroxidase, **human** eosinophilic peroxidase or **human** thyroid peroxidase.

DETD . . . peptide, preferably, however, of nucleic acid sequences which encode those part structures of which naturally occur in the precursors of **human** active compounds.

DETD . . . al., Mol. Cell Biol. 10, 2758 (1990); Berling et al., Cancer Res. 50, 3634 (1990)] or the signal sequence of **human** respiratory syncytial virus glycoproteins [cDNA of amino acids.from.seq.38 to .sqpreq.50 or 48 to 65; Lichtenstein et al., J. Gen. Virol.. . .

DETD . . . sequence.from.preq.51 to .storeq.107; Biemmann et al., Nature 342, 323 (1988)], is fused to component b), which contains the cDNA for **human** FX [nucleotide sequence 1 to .sqpreq.1668) [Messier et al., Gene 99, 291 (1991)] in which amino acid 194 has been. . .

DETD 3. Expression in **Human** Embryonic Kidney Cells

DETD Proliferating **human** embryonic kidney cells [HEK 293; Racchi et al., J. Biol. Chem. 264, 5755 (1989)] which are being maintained in culture. . .

DETD In this test, the coagulation defect in **human** FX-deficient plasma is counterbalanced by functionally active FXa.

DETD 3. Expression in **Human** Endothelial Cells

DETD **Human** umbilical cord endothelial cells which are being maintained in culture are transfected with the above-described plasmid using the method known. . .

I4 ANSWER 3 OF 16 USPATFULL

ACCESSION NUMBER:	2000:46389 USPATFULL
TITLE:	Modified protein for gene transfer and process for producing the same
INVENTOR(S):	Takehana, Yoshiyuki, Kawasaki, Japan Yamada, Naoyuki, Kawasaki, Japan Motoki, Masao, Kawasaki, Japan
PATENT ASSIGNEE(S):	Ajinomoto Co., Inc., Tokyo, Japan (non-U.S. corporation) Drug Delivery System Institute, Ltd., Tokyo, Japan (non-U.S. corporation)

	NUMBER	DATE
PATENT INFORMATION:	US 6013626	20000111
APPLICATION INFO.:	US 1997-927087	19970910 (8)
RELATED APPLN. INFO.:	Continuation of Ser. No. US 1995-536280, filed on 29 Sep 1995, now abandoned	

	NUMBER	DATE
PRIORITY INFORMATION:	JP 1994-270102	19940929

DOCUMENT TYPE:	Utility
PRIMARY EXAMINER:	Prieke, Scott D.
ASSISTANT EXAMINER:	Nguyen, Dave Trong
LEGAL REPRESENTATIVE:	Oblon, Spivak, McClelland, Maier & Neustadt, P.C.
NUMBER OF CLAIMS:	10

EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 4 Drawing Figure(s); 4 Drawing Page(s)
LINE COUNT: 698
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
SUMM ... a biologically active peptide or protein which can be bound to a specific receptor of a cell in a **human** body, and
SUMM ... and can transfer a nucleic acid into a specific type of cells, a specific organ or tumor cells of the **human** body.
SUMM When a nucleic acid is administered to the **human** body for gene therapy two difficulties arise. First, the nucleic acid is rapidly decomposed. Second, the DNA cannot easily enter. . .
DETD ...) **Human** red blood cells transglutaminase: Brenner et al, Biochem. Biophys. Acta. 521, 4-13 (1978).
DETD ... The substance should not be retained at any site in the circulatory system of the **human** body.
DETD ... The substance should not harm the **human** body.
DETD ... known. Examples include biologically active peptides obtained in the nature, for example, peptides which exhibit a physiological action in the **human** body, such as interleukin (IL -1, -2, -3, -4, -5, -6, -8, -9, -10 and -12, G-CSF, GM-CSF, . . .
DETD Antibodies are also biologically active peptides within the context of the present invention. Antibodies include not only **human** monoclonal antibodies but also animal monoclonal antibodies. Most of the biologically active peptides must specifically bind to their corresponding receptors. . . .
DETD ... In chronic rheumatism, a **lymphocyte** that expresses an **IL-6 receptor** is locally present and precipitates production of an auto-**antibody**, which leads to an attack or the progression of the disease.
DETD ... limited to polylysine. Any substances which is available and has some affinity for DNA, which is not harmful to the **human** body and which is not easily trapped in the circulatory system can be used.
DETD ... to stand at room temperature for 30 minutes. To the mixed solution were added 2 ml of rh IL-6 (recombinant **human** IL-6) solution, 2 ml of 10 mM sodium citrate, pH 7.0 . The mixture was stirred, and then allowed to stand. . .

L4 ANSWER 4 OF 16 MEDLINE DUPLICATE 1
ACCESSION NUMBER: 2000430[illegible] MEDLINE
DOCUMENT NUMBER: 10845614
TITLE: Increased T-lymphocyte interleukin-6 binding in patients with multiple sclerosis.
AUTHOR: Bongioanni P; Moretti S; Romano M F; Lombardo F; Moscato G; Meucci G
CORPORATE SOURCE: Department of Neurosciences, Section of Neurology; and Institute of Clinical Medicine, University of Pisa, Italy..
bongioanni@sirio.it
SOURCE: Eur J Neurol, (2000 May) 7 (3) 291-7.
Journal code: DAF. ISSN: 1351-5101.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200010
ENTRY WEEK: 20001004
AB ... nervous system associated with altered immunoregulation. Interleukin (IL)-6 is a cytokine that has several effects on the neuroimmune system. Specific **IL-6 receptors** have been found in **human lymphocytes** and neuroglial cells. The aim of the present study was to assay IL-6 binding on peripheral blood T **lymphocytes** in MS patients. We found that T cells from MS patients had significantly more **IL-6 receptors** [Bmax: 279 +/- 7 vs. 246 +/- 8 (mean +/- SEM)

receptors/cell, in patients and controls, respectively], whereas Kd values. . . 9 vs. 300 +/- 12 (mean +/- SEM) receptors/cell, respectively). We found significantly (P < 0.001) higher amounts of **IL-6 receptors** on CD4+ T cells from MS patients than on CD4+ **lymphocytes** from controls (434 +/- 11 vs. 363 +/- 9 (mean +/- SEM receptors/cell, respectively ; CD8+ T cells showed very few **IL-6 receptors** in both patients and controls. The data are discussed in terms of MS immune pathogenesis and pathophysiology, because T-cell activation seems to be linked to increased IL-6 binding. The upregulated IL-6 system might be involved in **antibody**-mediated demyelinating pathways, because IL-6 is well known to enhance humoral immune response.

CT Check Tags: Female; **Human**; Male
Adolescence
Adult
CD4-CD8 Ratio
CD4-Positive T-Lymphocytes: ME, metabolism
[illegible]-2: BL, blood
Interleukin-6: ME, metabolism
Middle Age
Multiple Sclerosis: BL,. . .

L4 ANSWER 5 OF 16 USPATFULL
ACCESSION NUMBER: 1998:44 03 USPATFULL
TITLE: Diagnosis and treatment of cancer having clonal macrophage involvement
INVENTOR(S): McGrath, Michael S., Burlingame, CA, United States
Seddiki, Brian, San Francisco, CA, United States
Shiramizu, Bruce, Pacifica, CA, United States
PATENT ASSIGNEE(S): University of California, San Francisco, San Francisco, CA, United States (U.S. corporation)

	NUMBER	DATE
PATENT INFORMATION:	US 5744 2	1998 4 28
APPLICATION INFO.:	US 1996-[illegible]1 63	19960215 (8)
RELATED APPN. INFO.:	Divis on of Ser. No. US 1994-286745, filed on 5 Aug 1994, now patented, Pat. No. US 5580715	
DOCUMENT TYPE:	Utility	
PRIMARY EXAMINER:	Chambers, Jasemine C.	
ASSISTANT EXAMINER:	Schmuck, Jill E.	
LEGAL REPRESENTATIVE:	Bret Field Boziecevic & Reed LLP; Bozicevic, Karl	
NUMBER OF CLAIMS:	5	
EXEMPLARY CLAIM:	1,5	
NUMBER OF DRAWINGS:	1 Drawing Figure(s); 1 Drawing Page(s)	
LINE COUNT:	1189	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

SUMM The field of the invention relates to cancer therapy; **human** immunodeficiency virus; recombinant macrophage; methods of diagnosis of macrophage involvement in cancer development; kits for use in diagnosis; and. . .

SUMM . . . In the cancer. Accord, the macrophage is substantially eliminated from the cancerous tissue by administering to the mammal (preferably a **human**) harboring the cancerous tissue, a therapeutic agent that is in a formulation for preferential uptake by a macrophage. The administering. . .

SUMM . . . germ inhibitor, and gelonin (Kuejun) (Lifson, J. D., et al., supra). Trichosanthin and momordharin inhibit expression of HIV antigens in **human** blood cells including macrophages (Lifson, J. D., et al., supra).

SUMM . . . Targeting moiety can be linked to a drug either directly or indirectly by carrier molecules such as serum albumin (particularly **human** serum albumin), polyaminoacids, dextran, and the like, by methods well known to those skilled in the art. The use of. .

SUMM . . . means an oncogene which increases the probability of the

development of neoplasms (particularly malignant tumors) in a mammal (particularly a **human**.. A gene associated with cell proliferation also includes a cell growth suppressing gene such that decreased gene expression of a. . .

SUMM By "HIV" is meant a **human** immunodeficiency virus of strains HIV-1, HIV-2, or other variants.

SUMM . . . of the invention are preferably designed for the diagnosis and treatment of clonal HIV- and non-HIV-associated macrophage-induced cancer in a **human**.

DETD . . . and hematopoietic (Akira, S. et al., Immunol Review (1992) 127:25-50). Many cell types, including monocyte/macrophages, fibroblasts, endothelial, B and T **lymphocytes**, chondrocytes, astrocytes and keratinocytes are capable of producing IL-6. IL-6 can exert growth-inhibiting, growth-inhibitory or differentiation inducing activities depending upon. . . cells. In regard to lymphocytic stimulation IL-6 has been shown to be involved in 1) terminal differentiation of B-cells into **antibody** producing plasma cells, 2) induction of IL-2 and IL-2 receptors and differentiation of T-cells; and 3 IL-6 has been shown. . . of myeloma and hybridoma cells. Woodrutt, G., et al., DNA and Cell Biology (1992) 11:587-592). IL-6 may cause transformation of **IL-6 receptor** expressing cells Tonyama, N., et al., J Exp Med (1990) 171:589). IL-6 producing macrophages and endothelial cells were shown to. . .

DETD . . . invention involves probing the restriction digested and gel separated DNA with nucleic acid probes that hybridize to specific mammalian (preferably, **human**) genomic DNA regions.

DETD SCID mice are infected with **human** splenic tissue containing clonal HIV-infected macrophages (e.g., tissue from Case 10). Control SCID mice are infected with normal or HIV. .

CLM What is claimed is:

. . . of a macrophage in vivo, said method comprising: a) injecting the macrophage of claim 1 into a tissue of a non-**human** mammal; b) growing said macrophage in said mammal until a tumor is present; c) administering to said mammal said candidate. . .

L4 ANSWER 6 OF 16 MEDLINE DUPLICATE 2

ACCESSION NUMBER: 98178234 MEDLINE

DOCUMENT NUMBER: 98178234

TITLE: Mechanism of growth control of Kaposi's sarcoma-associated herpes virus-associated primary effusion lymphoma cells.

AUTHOR: Asou H; Said J W; Yang E; Munker R; Park D J; Hamada N; Koeffler H P

CORPORATE SOURCE: Division of Hematology Oncology and Pathology, Cedars-Sinai Medical Center, UCLA School of Medicine, Los Angeles, CA 90048, USA.

CONTRACT NUMBER: 1CO1 CA 06911-02 (NCI)
CA 42710 (NCI)

SOURCE: BLOOD, 1998 Apr 1) 91 (7 2477-81.
Journal code: A8G. ISSN: 0006-4971.

PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals; Cancer Journals

ENTRY MONTH: 199806

ENTRY WEEK: 19980602

AB . . . (PDGF) may be important for survival of PE cells. However, little is known about the interaction of cytokines with KSHV-infected **lymphocytes** from PEL. Therefore, we investigated what cytokines were produced by KSHV-infected PEL cell lines (KS-1, BC-1, BC-2), what cytokine receptors. . . antisense oligonucleotides had no effect on two

B-cell lymphoma cell lines, which were not infected with KSHV. Addition of
IL-6 **antibody** did not inhibit clonal growth of any of the cell lines. Taken together, we have defined the cytokines and their receptors expressed on PEL cells and have found that these cells synthesized IL-6 and **IL-6 receptors**; interruption of this pathway by IL-6 antisense oligonucleotides specifically prevented the growth of these cells. These findings will offer potential. . .
CT Check Tags: **Human**; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.
Cell Division: DE, drug effects
Cytokines: PD, pharmacology
*Herpesvirus, Kaposi Sarcoma-Associated: IP, isolation. . .

L4 ANSWER 7 OF 16 MEDLINE DUPLICATE 3
ACCESSION NUMBER: 1998417561 MEDLINE
DOCUMENT NUMBER: 98417561
TITLE: IL-6 functions in cynomolgus monkeys blocked by a **humanized** antibody to **human** IL-6 receptor.
AUTHOR: Imaeda T; Saito E; Hasegawa M; Shinkura H; Kishimoto T; Ohsugi Y
CORPORATE SOURCE: Fuji-Gotemba Research Laboratories, Chugai Pharmaceutical Co., Ltd, Tokyo, Japan.
SOURCE: INTERNATIONAL JOURNAL OF IMMUNOPHARMACOLOGY, 1998 Jul) 20 ( ) 34 -37.
Journal code: GRI. ISSN: 0192-0561.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199809
ENTRY WEEK: 1998 -1
TI IL-6 functions in cynomolgus monkeys blocked by a **humanized** antibody to **human** IL-6 receptor.
AB A **humanized antibody** to the **human** interleukin-6 receptor (IL-6R), hPM-1, blocked the interleukin-6 (IL-6) functions in normal cynomolgus monkey **lymphocytes** in vitro. The binding activity of hPM-1 to non-**human** primate IL-6R was examined in peripheral blood **lymphocytes** by flow cytometry. PM-1 recognized the IL-6R on T **lymphocytes** of cynomolgus and rhesus monkeys, but did not on those of marmosets. The homology between **human** IL-6R and its cynomolgus monkey counterpart was 97.3% in the extracellular domain of the amino acid sequence, as determined by. . . blood mononuclear cells. PM-1 inhibited two functional parameters in vitro
in cynomolgus monkeys: (1), T-cell proliferation stimulated by phytohemagglutinin and **human** IL-6; (2), Immunoglobulin G-production induced by Staphylococcus aureus Cowan-I- and **human** IL-6-stimulated B **lymphocytes**. These data show that hPM-1 binds to and functionally blocks the cynomolgus monkey **IL-6 receptors**.
CT Check Tags: Animal; Comparative Study; **Human**
Amino Acid Sequence
Antibodies, Monoclonal: IM, immunology
*Antibodies, Monoclonal: PD, pharmacology
Base Sequence
Cell Line
[illegible]
Cross Reactions
[illegible]

L4 ANSWER 8 OF 16 MEDLINE DUPLICATE 4
ACCESSION NUMBER: 1998368076 MEDLINE
DOCUMENT NUMBER: 98368076
TITLE: T-cell interleukin-6 receptor binding in patients with

myasthenia gravis.

AUTHOR: Bingioanni P; Ricciardi R; Romano M R; Murri L; Muratorio A

CORPORATE SOURCE: Department of Neurosciences, University of Pisa, Italy.

SOURCE: JOURNAL OF THE NEUROLOGICAL SCIENCES, (1996 Jun 30) 136 (1-2) 213-20.
Journal code: JBJ. ISSN: 0022-510X.

PUB. COUNTRY: Netherlands
Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199701

ENTRY WEEK: 199710

AB Myasthenia gravis (MG) is a T-cell-dependent and **antibody**-mediated autoimmune disease of the neuromuscular function, in which the cytokine network may be deranged. Specific receptors for interleukin (IL)-6, a cytokine with several effects on the neuroimmune system, have been found on **human lymphocytes**. The aim of the present study has been to assay IL-6 binding on peripheral blood T cells from MG patients. We found that T cells from MG patients have significantly more **IL-6 receptors** than those from controls (Bmax: 334 +/- 6 vs 251 +/- 4 (mean +/- SEM) receptors/cell). Such IL-6 binding sites. . . (mean +/- SEM) pM). The enhanced T-cell interleukin-6 binding is due to an increased number of interleukin-6 receptors on T-helper **lymphocytes**. These results are discussed in terms of MG immunopathogenesis, since it has been reported that activated T cells have increased amounts of **IL-6 receptors**.

CT Check Tags: Female; **Human**: Male
Adult
Aged
Blood Cells: ME, metabolism
Lymphocyte Transformation: PH, physiology
Middle Age
*Myasthenia Gravis: BL, blood
Myasthenia Gravis: PA, . . .

L4 ANSWER 9 OF 16 USPATFULL

ACCESSION NUMBER: 97:51354 USPATFULL

TITLE: Diagnosis and treatment of cell proliferative disease having clonal macrophage involvement

INVENTOR(S): McGrath, Michael S., Burlingame, CA, United States
Bernheim, Brian, San Francisco, CA, United States
Shuramiru, Bruce, Pacifica, CA, United States

PATENT ASSIGNEE(S): The Regents of the University of California, Oakland, CA, United States (U.S. corporation)

	NUMBER	DATE
PATENT INFORMATION:	US 5639600	19970617
APPLICATION INFO.:	US 1995-473040	19950606 (8)
RELATED APPLN. INFO.:	Continuation-in-part of Ser. No. US 1994-286745, filed on 5 Aug 1994	

DOCUMENT TYPE: Utility

PRIMARY EXAMINER: Gibson, Bradley L.

LEGAL REPRESENTATIVE: Fortkevic, Gail Fish & Richardson P.C.

NUMBER OF CLAIMS: 11

EXEMPLARY CLAIM: 1

NUMBER OF DRAWINGS: 3 Drawing Figure(s); 2 Drawing Page(s)

LINE COUNT: 1711

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

SUMM The field of the invention relates to therapy for cell proliferative diseases; **human** immunodeficiency virus; a recombinant macrophage; methods of diagnosis of macrophage involvement in cell proliferative disease; kits for use in diagnosis;. . .

SUMM . . . the diseased tissue. Second, the macrophage is substantially eliminated from the diseased tissue by administering to the mammal (preferably a **human**) harboring the diseased tissue, a therapeutic agent that is in a formulation for preferential uptake by a macrophage. The administering. . .

SUMM . . . germ inhibitor, and gelonin (Vaidya, J. D., et al., supra). Trichosanthin and momordharin inhibit expression of HIV antigens in **human** blood cells including macrophages (Lifson, J. D., et al., supra).

SUMM . . . targeting moiety can be linked to a drug either directly or indirectly by carrier molecules such as serum albumin (particularly **human** serum albumin), polyaminoacids, dextran, and the like, by methods well known to those skilled in the art. The use of. . .

SUMM . . . means an oncogene which increases the probability of the development of neoplasms (particularly malignant tumors) in a mammal (particularly a **human**). A gene associated with cell proliferation also includes a cell growth suppressing gene such that decreased gene expression of a. . .

SUMM By "HIV" is meant a **human** immunodeficiency virus of strains HIV-1, HIV-2, or other variants.

SUMM . . . of the invention are preferably designed for the diagnosis and treatment of clonal HIV- and non-HIV-associated macrophage-induced cancer in a **human**.

DRWD FIG. 2 shows a schematic diagram of HIV insertion into **human** c-sis.

DRWD FIG. 3 is a portion of the **human** c-sis proto-oncogene sequence into which HIV has inserted at intron 1. The sequenced DNA was IPCR products from macrophages obtained. . .

DETD . . . and hepatocytes [Kaiho, S. et al., Immunol Review (1992) 127:5-6]. Many cell types, including monocyte/macrophages, fibroblasts, endothelia, B and T **lymphocytes**, chondrocytes, astrocytes and keratinocytes are capable of producing IL-6. IL-6 can exert growth-inducing, growth-inhibitory or differentiation inducing activities depending upon. . . cells. In regard to lymphocytic stimulation IL-6 has been shown to be involved in 1) terminal differentiation of B-cells into **antibody** producing plasma cells; 2) induction of IL-2 and IL-2 receptors and differentiation of T-cells; and 3) IL-6 has been known. . . of myeloma and hybridoma cells (Woodruff, C., et al., DNA and Cell Biology (1992) 11:587-592). IL-6 may cause transformation of **IL-6 receptor** expressing cells (Tohyama, K., et al., J Exp Med 1990) 171:389-9. IL-6 producing macrophages and endothelial cells were shown to. . .

DETD . . . invention involves probing the restriction digested and gel separated DNA with nucleic acid probes that hybridize to specific mammalian (preferably, **human**) genomic DNA regions.

DETD SCID mice are injected with **human** splenic tissue containing clonal HIV-1-infected macrophages (i.e., tissue from Case 1). Control SCID mice are injected with normal non-HIV. . .

DETD . . . derived growth factor B gene (PDGF-B) as shown in FIG. 3. A viral LTR sequence is shown inserted in the **human** c-sis gene (PDGF-B gene).

DETD . . . in experimental fat-fed rabbit systems (Rosenfeld, M. E. and Ross, R. (1990) Arteriosclerosis 10:656-687) and in cell cycle analysis of **human** plaques (Gordon, D. et al. (1990) P.N.A.S. U.S.A. 87:4600-4604), it is clear that in situ macrophage proliferation is comparable in. . .

DETD In **human** atherosclerotic lesions, PDGF-A and PDGF-B mRNA and protein are expressed in endothelial cells, smooth muscle cells, and macrophages (Barrett, T. . . .

DETD . . . from macrophages of the atherosclerotic plaque tissue. Using the v-cis probe (Oncor, Gathersberg, Md.) which hybridizes to sequences in the **human** PDGF-B gene, it was found that the PDGF-B gene was rearranged. Thus, the HIV insertion indicated by IPCR is shown. . . .

CLM What is claimed is:
. . . in a sample, wherein said method comprises: determining by a nucleic acid hybridization technique the presence in macrophage DNA of **human** immunodeficiency virus (HIV. integration at a location relative to a cell proliferative oncogene wherein said location is further characterized in. . .

L4 ANSWER 10 OF 16 BIOSIS COPYRIGHT 2000 BIOSIS
ACCESSION NUMBER: 1997:41[illegible] BIOSIS
DOCUMENT NUMBER: PREV199700702424
TITLE: Two-color flow cytometric analysis of cytokine receptors and surface markers on blood cells.
AUTHOR(S): Maruyama, Soichi (1); Aoki, Sadao; Tsukada, Nobuhiro; Nomoto, Hidehiko; Aizawa, Yoshifusa; Takahashi, Hoyu
CORPORATE SOURCE: (1) First Dep. Internal Med., Niigata Univ. Sch. Med., Asahi-machi Dori 1-757, Niigata 951 Japan
SOURCE: Acta Medica et Biologica, (1997) Vol. 45, No. 2, pp. 39-44.
ISSN: 03[illegible]
DOCUMENT TYPE: Article
LANGUAGE: English
AB. . . a specified cell population, two-color flow cytometric analysis of cytokine receptors and surface markers using fluorescence labeled cytokines and monoclonal **antibodies** was performed. In normal peripheral, blood cells, granulocytes expressed granulocyte colony-stimulating factor (G-CSF) receptor and interleukin-6 (**IL-6**) **receptor**, but mostly expressed interleukin-3 (IL-3) receptor weakly. Monocytes were positive for each receptor. In **lymphocytes**, CD3 positive T cells did not express any of these receptors; however, CD19 positive B cells expressed G-CSF receptor, IL-3 receptor, and partly expressed **IL-6 receptor**. In clinical cases, leukemic cells of acute myeloid leukemia (AML) patients tended to show the same characteristics as normal granulocytes. . .
IT Major Concepts
Biochemistry and Molecular Biophysics; Blood and Lymphatics (Transport and Circulation); Cell Biology; Clinical Immunology (**Human** Medicine, Medical Sciences); Endocrine System (Chemical Coordination and homeostasis); Hematology (**Human** Medicine, Medical Sciences); Membranes (Cell Biology); Oncology (**Human** Medicine, Medical Sciences)
OBGN Super Taxa
Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia
OBGN Organism Name
human (Hominidae)
OBGN Organism Superterms
animals; chordates; **humans**; mammals; primates; vertebrates

L4 ANSWER 11 OF 16 USPATFULL
ACCESSION NUMBER: 96:111806 USPATFULL
TITLE: Diagnosis of cancer having clonal macrophage involvement
INVENTOR(S): McGrath, Michael S., Burlingame, CA, United States
Kornbluth, Brian, San Francisco, CA, United States
Shiramizu, Bruce, Pacifica, CA, United States
PATENT ASSIGNEE(S): The Regents of the University of California, Oakland, CA, United States (U.S. corporation)

	NUMBER	DATE
PATENT INFORMATION:	US 5[illegible]071	19961203
APPLICATION INFO.:	US 1994-286741	19940805 (8)
DOCUMENT TYPE:	Utility	
PRIMARY EXAMINER:	Jones, W. Gary	
ASSISTANT EXAMINER:	Sisson, Bradley L.	
LEGAL REPRESENTATIVE:	Bozicevic, Karl	

NUMBER OF CLAIMS: 13
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 1 Drawing Figure(s); 1 Drawing Page(s)
LINE COUNT: 1207
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

SUMM The field of the invention relates to cancer therapy; **human** immunodeficiency virus; a recombinant macrophage; methods of diagnosis of macrophage involvement in cancer development; kits for use in diagnosis; and. . .

SUMM . . . in the cancer. Second, the macrophage is substantially eliminated from the cancerous tissue by administering to the mammal (preferably a **human** harboring the cancerous tissue, a therapeutic agent that is in a formulation for preferential uptake by a macrophage. The administering. . .

SUMM . . . germ inhibitor, and gelsonin (Xuejun) (Lifson, J. D., et al., supra). Trichosanthin and momorcharin inhibit expression of HIV antigens in **human** blood cells including macrophages (Lifson, J. D., et al., supra).

SUMM . . . targeting moiety can be linked to a drug either directly or indirectly by carrier molecules such as serum albumin (particularly **human** serum albumin), polyaminoacids, dextran, and the like, by methods well known to those skilled in the art. The use of. . .

SUMM . . . means an oncogene which increases the probability of the development of neoplasm (particularly malignant tumors) in a mammal (particularly a **human**). A gene associated with cell proliferation also includes a cell growth suppressing gene such that decreased gene expression of . . .

SUMM By "HIV" is meant a **human** immunodeficiency virus or strains HIV-1, HIV-2, or other variants.

SUMM . . . of the invention are preferably designed for the diagnosis and treatment of clonal HIV- and non-HIV-associated macrophage-induced cancer in a **human**.

DETD . . . and hematopoiesis (Akira, S. et al., Immunol Review (1992) 127:5-50). Many cell types, including monocyte/macrophages, fibroblasts, endothelia, B and T **lymphocytes**, chondrocytes, astrocytes and keratinocytes are capable of producing IL-6. IL-6 can exert growth-inducing, growth-inhibitory or differentiation inducing activities depending upon. . . cell. In regard to lymphocytic stimulation IL-6 has been shown to be involved in 1) terminal differentiation of B-cells into **antibody** producing plasma cells; 2) induction of IL-2 and IL-2 receptors and differentiation of T-cells; and 3) IL-6 has been shown. . . of myeloma and hybridoma cells (Woodruff, C., et al., DNA and Cell Biology (1992) 11:587-592). IL-6 may cause transformation of **IL-6 receptor** expressing cells (Tohyama, N., et al., J Exp Med (1992) 171:383). IL-6 producing macrophages and endothelial cells were shown to. . .

DETD . . . invention involves probing the restriction digested and gel separated DNA with nucleic acid probes that hybridize to specific mammalian (preferably, **human**) genomic DNA regions.

DETD SCID mice are injected with **human** splenic tissue containing clonal HIV-integrated macrophages (e.g., tissue from Case 10). Control SCID mice are injected with normal (no HIV. . .

CLM What is claimed is:

. . . macrophages from other cells of said sample; c) isolating DNA from said macrophages; and d) determining the presence of a **human** immunodeficiency virus (HIV) integrated into the fur gene.

5. The method of claim 1 wherein said **human** immunedeficiency virus is integrated into the z exon of the fur gene.

6. The method of claim 1 wherein said mammal is a **human**.

L4 ANSWER 12 OF 16 MEDLINE DUPLICATE 5

ACCESSION NUMBER: 93229747 MEDLINE
DOCUMENT NUMBER: 93229747
TITLE: Interleukin-6 inhibits the proliferation of B-chronic lymphocytic leukemia cells that is induced by tumor necrosis factor-alpha or -beta.
AUTHOR: Aderka D; Maor Y; Novick D; Engelmann H; Kahn Y; Levo Y; Wallach D; Revel M
CORPORATE SOURCE: Department of Molecular Genetics and Virology, Weizmann Institute of Science, Rehovot, Israel.
SOURCE: BLOOD, 1993 Apr 15) 81 (8 2076-84.
Journal code: A4B. ISSN: 0006-4971.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals; Cancer Journals
ENTRY MONTH: 199307
AB Tumor necrosis factor TNF-alpha acts as a growth stimulatory factor on leukemic B **lymphocytes** from many patients with chronic lymphocytic leukemia (CLL). Because TNF induces production of interleukin-6 (IL-6), which has been shown to . . . TNF on B-CLL cells. In fact, we found that IL-6 is an inhibitor of B-CLL growth. The addition of recombinant **human** IL-6 markedly decreased the TNF-induced B-CLL growth, and this decrease was even greater when soluble **IL-6 receptor**, known to act as IL-6 agonist, was added with recombinant IL-6. Conversely, neutralizing monoclonal **antibodies** to IL-6 and to the **IL-6 receptor** potentiated the growth stimulation of TNF on B-CLL cells, in line with the possibility that IL-6 functions as a negative. . .
CT Check Tags: Animal; **Human**; Support, Non-U.S. Gov't
B-Lymphocytes: ME, metabolism
B-Lymphocytes: PA, pathology
Cell Division
Cell Transformation, Viral
CHO Cells: ME, metabolism
Escherichia coli: ME, metabolism
Clusters
Herpesvirus 4, Human
Interleukin-6: IP, metabolism
*Interleukin-6: PD, pharmacology
*Leukemia, B-Cell, chronic: BL, blood
*Leukemia, B-Cell, chronic: PA, pathology
*Lymphotoxin: . . .

L4 ANSWER 13 OF 16 MEDLINE DUPLICATE 6
ACCESSION NUMBER: 93[illegible] MEDLINE
DOCUMENT NUMBER: 93[illegible]
TITLE: Effect of cell-derived growth factors and cytokines on the clonal outgrowth of EBV-infected B cells and established lymphoblastoid cell lines.
AUTHOR: Ottersen P; Zhang X M; Ohlin M; Zeuthen J; Borrebaeck C A
CORPORATE SOURCE: Department of Immunotechnology, Lund University, Sweden.
SOURCE: HUMAN ANTIBODIES AND HYBRIDOMAS, (1993 Jul) 4 (3) 115-23.
Journal code: A7A. ISSN: 0956-960X.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199312
AB Epstein-Barr virus (EBV) is a potent inducer of polyclonal B **lymphocyte** proliferation and is widely used as a tool for the establishment of B cell lines producing **human** monoclonal **antibodies**. However, because of low transformability, low clonability, and the inherent instability of EBV-infected B cells, valuable **antibody**-producing B cells are often lost during this

procedure. We have here examined various cell-derived cytokines for their ability to enhance. . . and monocyte cell lines were less capable than peripheral blood mononuclear cells in enhancing cellular outgrowth and cloning. Furthermore, the **human** T cell hybridoma cell line MP6 that secretes a B cell growth and differentiation factor, recently identified as an isoform. . . level. The present results also suggest that one potential role of the MP6-derived thioredoxin could be the up regulation of **IL-6 receptor** expression in EBV-transformed B cells.

CT Check Tags: **Human**; Support, Non-U.S. Gov't
B-Lymphocytes: DE, drug effects
B-Lymphocytes: MI, microbiology
*B-Lymphocytes: PH, physiology
Cell Line
Cell Line, Transformed
*Cell Transformation, Viral
*Cytokines: PD, pharmacology
DNA: BI, biosynthesis
*Growth Substances: PD, pharmacology
***Herpesvirus 4, Human: GE, genetics**
*Lymphocyte Transformation: DE, drug effects
Receptors, Immunologic: AN, analysis
Thioredoxin: PD, pharmacology

L4 ANSWER 14 OF 16 MEDLINE DUPLICATE 7
ACCESSION NUMBER: 9[illegible] MEDLINE
DOCUMENT NUMBER: 9[illegible]
TITLE: Expression of interleukin-6 receptor on blood lymphocytes without in vitro activation.
AUTHOR: [illegible]; Fleck L
CORPORATE SOURCE: Department of Clinical Immunology, Flinders Medical Centre, South Australia.
SOURCE: IMMUNOLOGY, (1992 Jun) 76 (2) 338-40.
Journal code: GBT. ISSN: 0019-2805.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
ENTRY MONTH: [illegible]

AB A monoclonal **antibody** against the interleukin-6 receptor (IL-6R) has been used in a high-sensitivity immunofluorescence technique to study receptor expression in unstimulated blood **lymphocytes**. Most CD4 cells express **IL-6 receptor**, whilst a small and variable proportion of CD8 and B cells are positive. CD4+ cells express higher levels of receptor. . .

CT Check Tags: **Human**
B-Lymphocytes: IM, immunology
CD4-Positive T-Lymphocytes: IM, immunology
*Lymphocytes: IM, immunology
*Receptors, Immunologic: AN, analysis
T-Lymphocytes: IM, immunology

L4 ANSWER 15 OF 16 MEDLINE DUPLICATE 8
ACCESSION NUMBER: 9[illegible] MEDLINE
DOCUMENT NUMBER: 9[illegible]
TITLE: IL-6 enhances the generation of cytolytic T lymphocytes in the allogeneic mixed leucocyte reaction.
AUTHOR: Metz J F; Steinman R M; Granelli-Piperno A
CORPORATE SOURCE: Laboratory of Cellular Physiology and Immunology, Rockefeller University, New York, NY 10021.
CONTRACT NUMBER: AI14775 (NIAID)
5-T32-GM07739 (NIGMS)
SOURCE: CLINICAL AND EXPERIMENTAL IMMUNOLOGY, (1992 Jul) 89 (1) 148-53.
Journal code: LD7. ISSN: 0009-9104.

PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
ENTRY MONTH: 199010

AB Cytolytic T **lymphocytes** (CTL) require soluble proteins termed lymphokines to develop lytic activity. In this report we have studied two of the lymphokines. . . . leucocyte reaction (MLR) High doses of dendritic cells induced lytic activity from purified CD8+ cells in both the murine and **human** MLR. Under these conditions, IL-2 and IL-6 were endogenously produced and secreted. **Antibodies** to IL-2 or the IL-2 receptor blocked CTL formation; however, anti-**IL-6 receptor antibodies** only partially inhibited the response while anti-IL-6 **antibodies** were largely ineffective. When limiting numbers of antigen-presenting cells were used CTL failed to develop, and neither IL-2 nor IL-6. . .

CT Check Tags: Animal; **Human**: Support, U.S. Gov't, P.H.S.
Antibodies: IM, Immunology
Cells, Cultured
Cytotoxicity, Immunologic
Dendritic Cells: IM, Immunology
Dendritic Cells: ME, metabolism
Dose-Response. . .

L4 ANSWER 16 OF 16 MEDLINE
ACCESSION NUMBER: 90179422 MEDLINE
DOCUMENT NUMBER: 90179422
TITLE: Production and secretion of BSF2/IL6 in a case of hairy cell leukemia with polyclonal hypergammaglobulinemia.
AUTHOR: Suda M; Hawanish. Y; Nakano M, Ohdo T; Toyama K
CORPORATE SOURCE: First Department of Internal Medicine, Tokyo Medical College.
SOURCE: NIPPON KETSUEKI GAKKAI ZASSHI. ACTA HAEMATOLOGICA JAPONICA,
(1989 May) 53 3 382-8.
Journal code: JSU. ISSN: 0001-5806.
PUB. COUNTRY: Japan
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: Japanese
ENTRY MONTH: 199010

AB . . . 8716 mg/dl . To elucidate the mechanism of the PHG, we investigated whether hairy cells produce interleukin 6 (IL-6) and express **IL-6 receptor.** The culture supernatant of these hairy cells increased [3H-]thymidine uptake of a IL-6 dependent hybridoma clone MH60 in a dose-dependent manner. These cells were stained with anti-IL-6 **antibody** using immuno-cytochemical technique. Our results suggested that these hairy cells produce and secrete IL-6. Immunocytochemical staining with anti **IL-6 receptor antibody** and the binding assay with [125I]-labelled recombinant IL-6 revealed that these cells express little or no receptors for IL-6. It . . . an autocrine growth factor for these cells but may play a role in development of PHG by stimulating normal B **lymphocytes** to produce an excessive amount of immunoglobulin.

CT Check Tags: Case Report; Female; **Human**; Support, Non-U.S. Gov't
B-Lymphocytes: IM, immunology
English Abstract
*Hypergammaglobulinemia: ET, etiology
*IgG
Interleukin-6: AN, analysis
*Interleukin-6: BI, biosynthesis
Interleukin-6: SE,. . .

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COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	28.31	28.52

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=> s il-6 and receptor and antibody and lymphocyte and treatment

L1 137 IL-6 AND RECEPTOR AND ANTIBODY AND LYMPHOCYTE AND TREATMENT

=> s (il-6 (s) receptor) and antibody and lymphocyte and treatment

L2 136 (IL-6 (S) RECEPTOR) AND ANTIBODY AND LYMPHOCYTE AND TREATMENT

=> s (il-6 (s) receptor) and antibody (p) lymphocyte (p) treatment

L3 19 (IL-6 (S) RECEPTOR) AND ANTIBODY (P) LYMPHOCYTE (P) TREATMENT

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L4 ANSWER 1 OF 21 MEDLINE DUPLICATE 1
ACCESSION NUMBER: 2000094687 MEDLINE
DOCUMENT NUMBER: PMID: 10594687
TITLE: Expression of functional interleukin-15 receptor and autocrine production of interleukin-15 as mechanisms of tumor propagation in multiple myeloma.
AUTHOR: Tinhofer I; Marschitz I; Henn T; Egle A; Greil R
CORPORATE SOURCE: Laboratory of Molecular Cytology, Department of Internal Medicine, University of Innsbruck, Innsbruck, Austria.
SOURCE: BLOOD, (2000 Jan 15) 95 (2) 610-8.
Journal code: AIG. ISSN: 0006-4971.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals; Cancer Journals
ENTRY MONTH: 200004

ENTRY WEEK: 20030401
AB Interleukin-15 (IL-15) induces proliferation and promotes cell survival of
human T and B **lymphocytes**, natural killer cells, and
neutrophils. Here we report the constitutive expression of a functional
IL-15 **receptor** (IL-15R) in 6 of 6 myeloma cell lines and in
CD38(high)/CD45(low) plasma cells belonging to 14 of 14 patients with. .
. the rate of spontaneous apoptosis, and the degree of this effect was
comparable to the pro-apoptotic effect of depleting autocrine **IL
-6** by **antibody** targeting. IL-15 was also capable of
substituting for autocrine **IL-6** in order to promote
cell survival and vice versa. In short-term cultures of primary myeloma
cells, the addition of IL-15. . . reduced the percentage of tumor
cells
spontaneously undergoing apoptosis. Furthermore, IL-15 lowered the
responsiveness to Fas-induced apoptosis and to cytotoxic **treatment**
with vincristine and doxorubicin but not with dexamethasone. These data
add IL-15 to the list of important factors promoting survival. . .

L4 ANSWER 2 OF 21 MEDLINE DUPLICATE 2
ACCESSION NUMBER: 20030289 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12909
TITLE: The engineered human anti-tumor necrosis factor-alpha
antibody CDP571 inhibits inflammatory pathways but not T
cell activation in patients with rheumatoid arthritis.
AUTHOR: Choy E H; Rankin E C; Kassamos D; Vetterlein O; Garyfallos
A; Farrington C T; Sopwith M; Eastell R; Kingsley G H;
Kennedy D A; Panayi G S
CORPORATE SOURCE: Department of Clinical and Molecular Rheumatology, The
Guy's Hospital Medical and Dental School, London, United
Kingdom.
SOURCE: JOURNAL OF RHEUMATOLOGY, 1999 Nov 26 (11) 2310-7.
Journal code: JWX. ISSN: 0315-162X.
PUB. COUNTRY: Canada
CLINICAL TRIAL
CONTROLLED CLINICAL TRIAL
Journal Article; JOURNAL ARTICLE
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200301
ENTRY WEEK: 20030101
AB OBJECTIVE: We investigated the effect of an engineered human anti-tumor
necrosis factor-alpha **antibody**, CDP571, on immune functions as
well as bone and cartilage turnover in patients with rheumatoid arthritis
(RA) in a placebo controlled trial. We also assessed the effects of
repeated **treatment** with CDP571 in an open label continuation
study. METHOD: Thirty-six patients were treated with either placebo or
0.1, 1, or 10 mg/kg of CDP571 given as an intravenous infusion. The
follow-up period was 8 weeks. **Lymphocyte** phenotype, soluble CD4
(sCD4), soluble interleukin 2 **receptor** (sIL-2R), **IL-
6**, and stromelysin levels in the blood were measured before and
after **treatment**; bone and cartilage markers (pyridinoline,
deoxypyridinoline, N-terminal telopeptide) were similarly assessed in the
urine. Patients who completed a placebo controlled trial of CDP571 were
offered further **treatment** with CDP571. They received a maximum
of 2 further doses of 1 mg/kg (7 patients) or 10 mg/kg (9 patients) in an
open study. RESULTS: Plasma **IL-6** level was
statistically significantly reduced in the 1 and 10 mg/kg groups. In the
10 mg/kg group, there were also. . . levels. Repeat doses of CDP571
were well tolerated and continued to suppress the acute phase response
and
disease activity. CONCLUSION: **Treatment** with 10 mg/kg of CDP571
reduced **IL-6** and surrogate markers of bone turnover in
RA, suggesting that CDP571 might prevent joint damage in RA. Since there
was no effect on **lymphocyte** markers despite the marked reduction
in inflammation, CDP571 appears to have no effect on ongoing CD4 T cell

activation.

L4 ANSWER 3 OF 21 MEDLINE DUPLICATE 3
ACCESSION NUMBER: [illegible] MEDLINE
DOCUMENT NUMBER: [illegible]
TITLE: Long-term follow-up of the changes in circulating cytokines, soluble cytokine receptors, and white blood cell subset counts in patients with rheumatoid arthritis (RA) after monoclonal anti-TNF alpha antibody therapy.
AUTHOR: Ohshima S; Saeki Y; Mima T; Sasai M; Nishioka K; Ishida H; Mukozu M; Suemura M; McCloskey R; Kishimoto T
CORPORATE SOURCE: Department of Molecular Medicine, Osaka University Medical School, Suita City, Japan.
SOURCE: JOURNAL OF CLINICAL IMMUNOLOGY, (1999 Sep) 19 (5) 305-13.
Journal code: HFD. ISSN: 0271-9142.
PUB. COUNTRY: United States
CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: [illegible]
ENTRY WEEK: [illegible]
AB To investigate the mechanism of the long-lasting efficacy of chimeric monoclonal anti-TNFalpha **antibody** (cA2) therapy for rheumatoid arthritis (RA), [illegible] patients with refractory RA were treated with a single infusion of cA2 and the changes in circulating cytokines (IL-1, **IL-6**, TNFalpha, and IL-10), soluble cytokine **receptors** (TNF-RI, RII, and sIL-6R) and peripheral white blood cell (WBC) subset counts were followed up long-term (12 weeks) after cA2. [illegible] all patients, as reported elsewhere. Moreover, five of the eight patients showed prolonged clinical responses (>12 weeks). The elevated serum **IL-6** and sTNF-RI (or RII) levels before **treatment** rapidly decreased after **treatment**. The serum IL-10 levels also significantly elevated before **treatment**. The elevations of serum IL-10 levels were augmented after **treatment** and stayed higher than the baseline in four patients with prolonged clinical responses. No significant TNFalpha, IL-1alpha and -beta, or IL-6R were detected in the sera of the patients before **treatment** and during the whole study period. On the other hand, peripheral **lymphocytes** as well as total WBC and neutrophils increased for 4 weeks after **treatment**. However, thereafter, only the **lymphocyte** count decreased gradually and stayed below the baseline long-term (12 weeks). FACS analysis revealed the predominance of T **lymphocytes** in the decrease in **lymphocyte** counts. These results suggest that the augmentation of IL-10 production and the decrease in T cells might partly contribute to the long-lasting efficacy of cA2 **treatment** in RA.

L4 ANSWER 4 OF 21 MEDLINE DUPLICATE 4
ACCESSION NUMBER: [illegible] MEDLINE
DOCUMENT NUMBER: [illegible]
TITLE: Cytokines in inflammatory bowel disease.
AUTHOR: Ziegler S; Andus T
CORPORATE SOURCE: Department of Internal Medicine I, University of Regensburg, Germany.
SOURCE: WORLD JOURNAL OF SURGERY, (1998 Apr) 22 (4) 382-9. Ref: [illegible]
Journal code: WJS. ISSN: 0364-2313.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
General review; (REVIEW)
(REVIEW, ACADEMIC)
LANGUAGE: English

ENTRY MONTH: 199806
ENTRY WEEK: 199804

AB Cytokines play a central role in the modulation of the intestinal immune system. They are produced by **lymphocytes** (especially T cells of the Th1 and Th2 phenotypes), monocytes, intestinal macrophages, granulocytes, epithelial cells, endothelial cells, and fibroblasts. They have proinflammatory functions [interleukin-1 (IL-1), tumor necrosis factor (TNF), **IL-6**, IL-8, IL-12] or antiinflammatory functions [interleukin-1 **receptor** antagonist (IL-1ra), IL-4, IL-10, IL-11, transforming growth factor beta (TGF beta)]. Mucosal and systemic concentrations of many pro- and antiinflammatory. . . acid (TNBS) model, or the genetically engineered model of IL-10 knockout mice. Based on these findings a rationale for cytokine **treatment** was defined. The first clinical trials using neutralizing monoclonal **antibodies** against TNF alpha (cA2) or the antiinflammatory cytokine IL-10 have shown promising results. However, many questions must be answered before. . .

L4 ANSWER 5 OF 21 MEDLINE DUPLICATE 5
ACCESSION NUMBER: 97318910 MEDLINE
DOCUMENT NUMBER: 97318910
TITLE: Decreased expression of ICAM-1 and its induction by tumor necrosis factor on breast-cancer cells in vitro.
AUTHOR: Endrissy A I; Brodowicz T; Wiltschke C; Czerwenka K; Michl I; Kubista M; Zielinski C C
CORPORATE SOURCE: Department of Internal Medicine I, University Hospital, Vienna, Austria.
SOURCE: INTERNATIONAL JOURNAL OF CANCER, (1997 Jun 11) 71 6) 1086-90.
Journal code: GQH. ISSN: 0020-7136.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
ENTRY MONTH: 199726
ENTRY WEEK: 199706

AB . . . lower than that of benign breast cells or normal breast epithelium. Of various cytokines tested, including recombinant human (rh) interleukin-6 (**IL-6**), rh tumor necrosis factor alpha (TNF-alpha), interleukin-1 (IL-1), granulocyte/macrophage-colony-stimulating-factor (GM-CSF), interferon-alpha (IFN-alpha) and interferon-gamma (IFN-gamma), only TNF was able. . . unstimulated or lymphokine-stimulated killer (LAK) cells to recognize and lyse native or TNF-stimulated breast-cancer cells was studied. Whereas neither unstimulated **lymphocytes** or LAK cells were able to lyse untreated breast-cancer cells sufficient for ICAM-1 expression, pre-**treatment** of tumor cells with TNF led to increased tumor-cell lysis. Anti-ICAM-1 **antibodies**, and pre-**treatment** of tumor cells with anti-TNF-**receptor antibodies**, abrogated these findings, corroborating their specificity. We thus conclude that the effective expression of ICAM-1 in our model might constitute. . .

L4 ANSWER 6 OF 21 MEDLINE DUPLICATE 6
ACCESSION NUMBER: 97414636 MEDLINE
DOCUMENT NUMBER: 97414636
TITLE: Medroxyprogesterone acetate reduces the in vitro production of cytokines and serotonin involved in anorexia/cachexia and emesis by peripheral blood mononuclear cells of cancer patients.
AUTHOR: Mantovani G; Maccio A; Esu S; Lai P; Santona M C; Massa E; Lusso M D; Melis G B; Del Giacco G S
CORPORATE SOURCE: Department of Medical Oncology, University of Cagliari, Italy.

SOURCE: EUROPEAN JOURNAL OF CANCER, (1997 Apr) 33 (4) 602-7.
Journal code: ARV. ISSN: 0959-8049.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
ENTRY MONTH: 199711
ENTRY WEEK: 19971104

AB Medroxyprogesterone acetate MPA is widely used in oncology both in the **treatment** of hormone-related cancers and as supportive therapy in anorexia/cachexia syndrome (ACS , but conclusive data are not yet available to explain . . . it characterised by weight loss, changes in metabolism, reduction of appetite, nausea and vomiting. Several cytokines,
mainly interleukin 1IL-1, IL-6, **IL-6** and tumour necrosis factor alpha TNF alpha , are involved in the pathogenesis of ACS. Additionally, nausea and vomiting can be mediated by factors inducing
serotonin (5-HT) production and/or release by enterotropic cells including activated T **lymphocytes**. In the present study, we report the effect of MPA on peripheral blood mononuclear cells (PBMC) from 10 cancer patients. . . (5 head and neck, 3 colon, 1 lung and 1 ovary). The proliferative response of PBMC to PHA, anti-CD3 monoclonal **antibody** MAb) or recombinant IL-2 (rIL-2 , the production of IL-1 beta, IL-2, **IL-6**, TNF alpha and 5-HT by PHA-stimulated PBMC and the expression of **lymphocyte** membrane-bound IL-2 **receptor** IL-2R) subunits CD25 and CD122) were studied. The addition of MPA significantly reduced the PBMC proliferative response to PHA and anti-CD3 MAb but not to rIL-2. MPA 0.2 microgram/mL was also capable of reducing the levels of IL-1 beta, **IL-6**, TNF alpha and 5-HT produced in culture by PHA-stimulated PBMC, whereas it did not induce any change in the percentage . . .

L4 ANSWER 7 OF 11 MEDLINE DUPLICATE 7
ACCESSION NUMBER: 97201264 MEDLINE
DOCUMENT NUMBER: 97201264
TITLE: A comparative study of the in vitro immunomodulatory activity of human intact immunoglobulin (7S IVIG), F(ab')2 fragments 5S IVIG and Fc fragments. Evidence for post-translational IL-2 modulation.
AUTHOR: Nambaur S; Herold M; Eibl B; Glass. H; Schwaighofer H; Huber C; Fachter A; Pichl M; Niederwieser D
CORPORATE SOURCE: Department of Internal Medicine, University Hospital, Innsbruck, Austria.
SOURCE: IMMUNOLOGY, (1997 Feb) 90 (2) 212-8.
Journal code: GHT. ISSN: 0019-2805.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
ENTRY MONTH: 199705
ENTRY WEEK: 19970504

AB During the past few decades intravenous immunoglobulin (IVIG) has been used successfully in the **treatment** of various immunoregulatory disorders. **Treatment** results have been attributed to immunomodulation mainly via Fc **receptors** or by anti-idiotypic **antibodies** to disease-causing autoantibodies. From the present study it is clearly evident that 7S IVIG (intact immunoglobulin as well as F(. . . have a potent immunomodulatory capability. We demonstrate that
mainly 7S IVIG inhibits alloantigen-induced T-cell proliferation and generation of cytotoxic T **lymphocytes**. Reduced interleukin-2 (IL-2) protein levels in culture supernatants of IVIG-supplemented mixed **lymphocyte** reactions MLR) but unchanged IL-2 mRNA levels strongly argue in favour of a post-transcriptional interference of IVIG with cytokines and/or cytokine production. Interferon-gamma (IFN-gamma),

soluble IL-2 **receptor** (sIL-2R) and monokines such as IL-1 beta, **IL-6**, IFN-alpha and tumour necrosis factor (TNF-alpha) were not affected by IVIG supplementation to MLR. Fc fragments were superior to F(ab')2-containing. . .

L4 ANSWER 8 OF 21 MEDLINE DUPLICATE 8
ACCESSION NUMBER: [illegible] MEDLINE
DOCUMENT NUMBER: [illegible]
TITLE: [illegible] functional analysis of an autoantigen reactive B cell clone
derived from MRL/MP-lpr/lpr mice.
AUTHOR: Hobayashi K; Hamano T; Makishima E
CORPORATE SOURCE: [illegible] Department of Internal Medicine, Hyogo College of Medicine.
SOURCE: NIPPON [illegible] (1996 Dec) 36 (6) 844-55.
Journal code: [illegible]. ISSN: 0300-9157.
PUB. COUNTRY: Japan
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: [illegible]
ENTRY MONTH: [illegible]
ENTRY WEEK: [illegible]
AB . . . provide a good model for the study on the pathogenesis of systemic lupus erythematosus with massive involvement of abnormal T **lymphocytes** in the spleen and lymphonodes. However, a direct role of B cells of MRL/lpr mice in autoimmune responses is not. . . exhibit rosette formation against blood cells treated with bromelain (Br-RBC) at a frequency of more than 90%, and to express DNA-**receptor** (DNA-R) on its surface by FCM analysis with biotin-labeled ssDNA. In contrast, the parental 2.52 M did not form rosettes. . . membrane of 2.52 M was significantly less compared with that of MRL27.4. Interestingly, MRL27.4 produced a high titer of IgM-anti-ssDNA **antibodies** and **IL-6** after **treatment** with the purified Br-RBC membrane fraction. On the other hand, the parental 2.52 M neither produce IgM-anti-ssDNA **antibodies** nor **IL-6** under the same conditions. The results suggest that MRL27.4 is an autoantigen reactive B cell clone derived from MRL/lpr mice. . . and its surface DNA-R, by itself, functions to autoantigens. In this process, there might be an autocrine network mediated by **IL-6**. In conclusion, MRL27.4 provides a good model for the study on the direct function of B cells of MRL/lpr mice. . .

L4 ANSWER 9 OF 21 MEDLINE DUPLICATE 9
ACCESSION NUMBER: [illegible] MEDLINE
DOCUMENT NUMBER: [illegible]
TITLE: IFN-alpha-mediated suppression of low-affinity Fc(epsilon) receptors on Peyer's patch lymphocytes and augmentation of soluble CD23: implications for IgE responses.
AUTHOR: [illegible]; Bluth M H; Chico S M; Durkin H G; Auci D L
CORPORATE SOURCE: Department of Pathology, State University of New York Health Science Center at Brooklyn, 11203, USA.
SOURCE: JOURNAL OF LEUKOCYTE BIOLOGY, (1996 May) 59 (5) 725-7.
Journal code: [illegible]. ISSN: 0741-5400.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
ENTRY MONTH: [illegible]
AB The ability of interleukin (**IL**)-6 or interferon-alpha (IFN-alpha) to modulate expression of low-affinity Fc(epsilon) **receptor** (CD23) and serum levels of sCD23 was studied in benzylpenicilloyl-keyhole limpet hemocyanin-sensitized BALB/c mice at the peak of a hapten-specific immunoglobulin E (IgE) **antibody** -forming cell (AFC) response. These responses are analogous to those

observed in human atopic disease. To induce peak IgE responses, mice. . . micrograms) in aluminum hydroxide gel (alum) on days 0, 21, and 42. On day 44, mice were injected subcutaneously with **IL-6** (100-1000 U) or IFN-alpha (1000-10,000 U). On day 46, numbers of CD23+ **lymphocytes** in Peyer's patches (PP), mesenteric lymph nodes (MLN), and spleen and levels of soluble CD23 in serum were determined (flow. . . assay, confirmed by competitive assay). Data are expressed as percent total cells or as optical density at 490 nm. IFN-alpha **treatment** strongly suppressed up to 10-fold numbers of CD23+ cells exclusively in PP (i.e., numbers of CD23+ cells in MLN and spleen were unchanged) whereas serum levels of soluble CD23 were dramatically increased (60%). **IL-6 treatment** had no effect on either numbers of CD23+ **lymphocytes** or on serum levels of soluble CD23. The data suggest that the mechanisms by which IFN-alpha, but not **IL-6**, regulates IgE responses involves suppression of CD23 expression on **lymphocytes** in PP and supports a central role for these organs in regulation of IgE responses in vivo.

L4 ANSWER 10 OF 21 MEDLINE DUPLICATE 10
ACCESSION NUMBER: 96187891 MEDLINE
DOCUMENT NUMBER: 96187891
TITLE: Anti-CD3 monoclonal antibody-induced receptor changes. II. Interaction of CD2 and CD3.
AUTHOR: Lin J; Chavin K D; Pan L; Dang Y; Bromberg J S
CORPORATE SOURCE: Department of Surgery, University of Michigan, Ann Arbor 48109, USA.
CONTRACT NUMBER: AI33515 (NIAID)
SOURCE: MOLECULAR IMMUNOLOGY, (1996 Feb) 33 (2) 249-58.
Journal code: C39. ISSN: 0161-5890.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Index Journals
ENTRY MONTH: 199603
AB Anti-CD3 monoclonal **antibodies** (mAbs) and anti-CD2 mAbs each prolong allograft survival and cause transient downmodulation of homologous **receptor** expression. Anti-CD3 mAb also act synergistically with anti-CD2 mAbs to prolong allograft survival and induce tolerance. The effect of combined anti-CD2 and anti-CD3 mAb **treatment** on **receptor** expression was further analyzed with an in vitro model. The anti-CD3 mAb 145-2C11 caused CD2 expression on purified splenic T. . . decreasing CD3 expression [69.1% (3.47) to 54.9% (2.37)]. Modulation of CD2 and CD3 expression was similar on mixed splenic T **lymphocytes** and isolated CD4 and CD8 subsets. Modulation did not change with the addition of the cytokines IL-1, IL-2, IL-4, **IL-6**, IL-10, TNF alpha, or TGF beta. Kinetic studies showed that modulation of CD2 was rapid, persistent, and of the same. . . magnitude from day 1 to Day 7 of culture while CD3 downmodulation was transient. The results of transcriptional analysis and **receptor** distribution suggested that downmodulation was due to **receptor** internalization while upregulation was due to increased transcription. Analysis of expression of other adhesion molecules demonstrated that CD11a, CD18, CD44,. . . and CD3 expression on T cells and modulation is accompanied by changes in the array of other T cell surface **receptors**. Changes in cell surface **receptor** display may provide an additional explanation for the synergistic effect of anti-CD2 plus anti-CD3 in prolonging allograft survival.

L4 ANSWER 11 OF 21 MEDLINE DUPLICATE 11
ACCESSION NUMBER: 97020558 MEDLINE
DOCUMENT NUMBER: 97020558
TITLE: 15-Hydroxyspergualin inhibits interleukin 6 production in in vitro stimulated human lymphocytes.
AUTHOR: Berg A J; Kumagai-Braesch M; Moller E
CORPORATE SOURCE: Department of Immunology, Microbiology, Pathology and

Infectious Diseases, Karolinska Institute, Huddinge Hospital, Sweden.
SOURCE: TRANSPLANT IMMUNOLOGY, (1996 Jun) 4 (2) 133-43.
Journal code: B3J. ISSN: 0966-3274.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journal
ENTRY MONTH: 199704

AB Experimental data show that relatively low concentrations of 15-deoxyspergualin (DSG) inhibit the induction of cytotoxic T **lymphocytes** (CTL) and the generation of **antibody**-producing cells. Considerably higher concentrations of DSG are required to inhibit proliferative responses. In this in vitro study, the effects of . . . DSG on CTL induction, on proliferative responses induced by different stimuli, and on the production of interleukins IL-1, IL-2 and **IL-6** and IFN-gamma (gamma-interferon) were assessed and compared with the effects of CsA (cyclosporine A) and/or FK506. We confirmed the suppressive . . . the generation of CTL. Quite unexpectedly, however, we found that, although DSG did not affect the proliferative response to allogeneic **lymphocytes** or a superantigen, it did inhibit proliferation of peripheral blood leucocytes (PBL) stimulated with Staphylococcus aureus. DSG was active even . . . lower in cells stimulated by S. aureus in the presence of DSG, showing a selective effect on CD8+CD4+ responder T **lymphocytes**. The proportion of IL-2 **receptor** (CD25) positive cells was also reduced by DSG **treatment**. Moreover, we found that DSG inhibited the proliferation induced by PHA (phytohaemagglutinin) but not by Con A (concanavalin A). Thus, . . . CD8-mediated pathway. DSG did not influence the production of IL-2 or IFN-gamma or the lipopolysaccharide induced production of IL-1 or **IL-6**. In contrast, the production of **IL-6** was inhibited when cells were stimulated by allogeneic **lymphocytes**, S. aureus, PHA or Con A. This suggested that the DSG-suppressed **IL-6** production could be the basis for the other observed effects. We tried to mimic the DSG effects with **antibodies** and indeed found that the **IL-6** specific **antibodies** had similar effects. Furthermore, recombinant **IL-6** completely overcame the suppressive effects of DSG on S. aureus and PHA induced proliferation, whereas addition of **IL-6** to DSG treated PBL only partly restored the cytotoxic activity of lymphoblasts induced by allogeneic cells. Thus, the inhibitory effect of DSG on de novo synthesis of **IL-6** could explain some of its immunosuppressive effects, but additional DSG-sensitive steps are obviously involved in CTL induction and differentiation.

L4 ANSWER 12 OF 21 MEDLINE DUPLICATE 12
ACCESSION NUMBER: 96117011 MEDLINE
DOCUMENT NUMBER: 96117011
TITLE: Selective immunomodulation in patients with inflammatory bowel disease--future therapy or reality?.
AUTHOR: van Hogezand R A; Verspaget H W
CORPORATE SOURCE: Department of Gastroenterology-Hepatology, University Hospital Leiden, Netherlands.
SOURCE: NETHERLANDS JOURNAL OF MEDICINE, (1996 Feb) 48 (2) 64-7.
Ref: 21
Journal code: NWY. ISSN: 0300-2977.
PUB. COUNTRY: Netherlands
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
ENTRY MONTH: 199703
ENTRY WEEK: 19970304

AB . . . has not so far been elucidated. In theory, an antigen-presenting

cell forms a complex with endotoxin-derived peptides as antigen. T-helper **lymphocytes** recognize this complex, are activated and start to produce cytokines. For inflammatory bowel diseases (IBD) the most important cytokines identified are interleukin 1 (IL-1), interleukin 2 (IL-2), interleukin 6 (**IL-6**), interleukin 8 (IL-8), gamma-interferon (gamma-IFN), and tumor necrosis factor-alpha (TNF-alpha). Inhibition of these cytokines can be achieved by administration of cyclosporine, which inhibits the function of T-helper **lymphocytes**. Orally, intravenously, and locally administered cyclosporine is able to improve the disease activity in ulcerative colitis and Crohn's disease, but. . . immunosuppressant FK506 has comparable actions to cyclosporine in regulating cytokine production and may even be more effective than cyclosporine. The **receptor** antagonist of IL-1 (IL-1ra) competitively binds to the IL-1 **receptor** located on several **lymphocytes**. **Treatment** of animals with IL-1ra has been successful and clinical trials using recombinant IL-1ra are underway in IBD. **Antibodies** against alpha-IL-2 have also been used successfully in animal studies. No experience with this substance has been obtained in man. The use of alpha-interferon seems to be effective in some patients with Crohn's disease. CD4 and CD8 molecules on **lymphocytes** are needed to form the interaction between antigen, antigen-presenting cell, and **lymphocytes**. Specific monoclonal **antibodies** against CD4 are successfully used in patients with active ulcerative colitis and Crohn's disease. TNF-alpha shares many of the proinflammatory activities of IL-1. In preliminary studies, especially in patients with Crohn's disease, the effects of the administration of **antibodies** to TNF-alpha were excellent.

L4 ANSWER 13 OF 21 MEDLINE DUPLICATE 13
ACCESSION NUMBER: 96152717 MEDLINE
DOCUMENT NUMBER: 96152717
TITLE: Antibody-targeted superantigen therapy induces tumor-infiltrating lymphocytes, excessive cytokine production, and apoptosis in human colon carcinoma.
AUTHOR: Dohlsten M; Dohlsten U; Lando P A; Halland T; Onisson L; Andersson J; Andersson U
CORPORATE SOURCE: Department of Immunology, Arrhenius Laboratory for Natural Sciences, Stockholm University, Sweden.. mark@imm2.su.se
SOURCE: EUROPEAN JOURNAL OF IMMUNOLOGY, (1996 Jan) 26 (1) 1-9. Journal code: EN5. ISSN: 0014-2980.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
ENTRY MONTH: 199603

AB Bacterial superantigens are the most potent known activators of human T **lymphocytes**. To engineer superantigens for immunotherapy of human colon carcinoma, the superantigen, staphylococcal enterotoxin A (SEA) was genetically fused to the Fab region of the colon carcinoma-reactive monoclonal **antibody** C242. In the present study the effector mechanisms involved in the anti-tumor response to C242 Fab-SEA were characterized. Immunohistochemistry and. . . IL-4, IL-5, IL-10, IL-12, interferon (IFN)-gamma, granulocyte-macrophage colony-stimulating factor, and transforming growth factor-beta, whereas IL-1-alpha, IL-1ra, IL-1 beta, TNF-beta, IL-6, **IL-6**, and IL-8 were undetectable. Most of the TNF-alpha, IL-2, IL-12, and IFN-gamma were made by the infiltrating human leukocytes, while the colon carcinoma cells were induced to produce IL-4, IL-10, and TNF-alpha. Up-regulation of IFN-gamma **receptors** and TNF R p60 **receptors** was found, while the TNF R p80 **receptor** was absent. The cytokine production, T cell infiltration, and CD95 Fas **receptor** expression concomitantly

occurred to induce programmed cell death in the tumor cells. This was followed by a strong reduction of the tumor mass that was seen within 24 h after 2242 Fab-SEA infusion. These findings demonstrate that **antibody**-superantigen proteins efficiently recruit tumor-infiltrating **lymphocytes** actively producing a variety of cytokines likely to be essential for the therapeutic effects observed in the model. Although the humanized SCID model has obvious limitations in its predictive value for **treatment** of human cancer, we believe that these results encourage clinical evaluation of **antibody**-targeted superantigens.

L4 ANSWER 14 OF 21 MEDLINE DUPLICATE 14
ACCESSION NUMBER: 95193051 MEDLINE
DOCUMENT NUMBER: 95193051
TITLE: CD38 ligation induces discrete cytokine mRNA expression in human cultured lymphocytes.
AUTHOR: Iagaletta C M; Urbani F; La Sala A; Funaro A; Malavasi F
CORPORATE SOURCE: Laboratorio di Batteriologia e Micologia Medica, Istituto Superiore di Sanita, Roma, Italy.
SOURCE: EUROPEAN JOURNAL OF IMMUNOLOGY, (1995 May) 25 (5) 1477-80. Journal code: EN5. ISSN: 0014-2980.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
ENTRY MONTH: 199509
AB Human CD38 is a surface glycoprotein expressed by different immune-competent cells such as immature and activated **lymphocytes**, plasma cells and natural killer cells. It has recently been reported that the CD38 molecule exerts adenosine diphosphate ribosyl cyclase activity and is associated with distinct transmembrane signaling molecules. This study reports that ligation of CD38 by specific monoclonal **antibodies** (mAb) induces multiple cytokine mRNA expression in cultured peripheral blood mononuclear cells (PBMC). The mRNA for tumor necrosis factor-alpha, interleukin (IL)-1 beta, **IL-6**, granulocyte-macrophage colony-stimulating factor (GM-CSF), and IL-12 were always detected, whereas interferon-gamma and IL-1 mRNA expression were seen in most, but . . . between CD38 and CD3 activation are the low to undetectable levels of IL-2 mRNA, and the sustained IL-1 beta and **IL-6** mRNA accumulation found in PBMC cultures following **treatment** with anti-CD38 mAb. Furthermore, PBMC proliferation was not found to be a prerequisite for CD38-mediated cytokine induction. Together, these results. . . induction of a discrete array of cytokines, and that this pathway only partially overlaps with that controlled by T cell **receptor** CD3.

L4 ANSWER 15 OF 21 MEDLINE DUPLICATE 15
ACCESSION NUMBER: 95150171 MEDLINE
DOCUMENT NUMBER: 95150171
TITLE: Anti-CD2 monoclonal antibody-induced receptor changes: down
modulation of cell surface CD2.
AUTHOR: Lin J; Von E W; Chavin K D; Qin L; Woodward J; Ding Y; Vaitis H; Bromberg J S
CORPORATE SOURCE: Department of Microbiology, Medical University of South Carolina, Charleston 29425, USA..
CONTRACT NUMBER: AI-06 5 (NIAID)
SOURCE: TRANSPLANTATION, (1995 Apr 27) 59 (8) 1162-71
Journal code: WEI. ISSN: 0041-1337.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
ENTRY MONTH: 199508

AB . . . LFA-1 beta (CD18), Pgp-1 (CD44), CD45, MEL-14 (L-selectin), and VLA-4 alpha (CD49d), were all increased as a result of anti-CD2 **treatment**, whereas CD25 (IL-2R), CD48 (CD2 ligand), and ICAM-1 (CD54) remained unchanged. Kinetics showed that CD2 down-modulation was persistent and at . . . for day 1 through day 7 of culture. Anti-CD2 mAb could down-regulate CD2 on both CD4 and CD8 splenic **lymphocyte** subsets, thymocytes, and the T cell lymphoma EL-4; and, non-T cells did not seem to participate in the process of . . . of T cell CD2 expression in an epitope and isotype dependent fashion and that CD2 down-modulation correlated with inhibition of **receptor**-driven T cell stimulation. Intact **antibody**, including the Fc portion, was required to induce CD2 down-modulation, and additional experiments suggested an interaction with an Fc gamma. . . Fc gamma RII or Fc gamma RIII. CD2 down-modulation did not change with the addition of the cytokines IL-1, IL-4, **IL-6**, IL-10, TNF alpha, or TGF-beta 1. These results show that anti-CD2 mAbs significantly and persistently down-regulate CD2 on various T cell subpopulations. The mAbs must interact with both the CD2 **receptor** and an Fc gamma R. CD2 down-modulation is accompanied by changes in the array of other T cell surface **receptors** that may contribute to mechanisms of anti-CD2-induced immunosuppression.

L4 ANSWER 16 OF 21 MEDLINE
ACCESSION NUMBER: 1[illegible] MEDLINE
DOCUMENT NUMBER: [illegible]
TITLE: Clinical and immunological follow-up of patients with AIDS-associated Kaposi's sarcoma treated with an anti-IL-6 monoclonal antibody.
AUTHOR: Rossi E; Audhuy B; Devernoy N; Thyss A; Lang J M; Wijdenes J; Herve P
CORPORATE SOURCE: Centre de Transfusion Sanguine, Besancon, France.
SOURCE: CYTOKINES AND MOLECULAR THERAPY, (1995 Jun) 1 (2) 133-8. Journal code: [illegible]. ISSN: 1355-0568.
PUB. COUNTRY: ENGLAND: United Kingdom
(CLINICAL TRIAL
Journal; Article; JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: [illegible]
ENTRY WEEK: [illegible]
AB . . . in stage III b and one in stage IV of the disease) were treated for 14 days with B-F8, an anti-**IL-6** monoclonal **antibody** (IgG1), at a daily dose of 10 mg. No side-effects were observed, but no patients experienced a complete or partial response. No modification was noted in the analysis of **lymphocyte** subsets, except for a transient decline in the number of cells expressing CD56, accompanied by altered NK activity in four of the seven evaluable patients. Anti-**IL-6** mAb prevented the binding of **IL-6** to its cell membrane **receptor**, as documented by the decline in C reactive protein levels. However, anti-**IL-6** mAb induced the circulation of significant amounts of **IL-6**, probably in the form of monomeric immune complexes. The sera, analysed on B9 cell line, demonstrated a stimulating activity, indicating that hypersensitive cells were able to cleave these complexes. This observation, together with the clinical inefficacy of the **treatment**, should prompt us to be careful with the use of unmanipulated single monoclonal **antibodies**, especially in cancer patients.

L4 ANSWER 17 OF 21 MEDLINE DUPLICATE 16
ACCESSION NUMBER: 94[illegible] MEDLINE
DOCUMENT NUMBER: 94029211
TITLE: Combination anti-CD2 and anti-CD3 monoclonal antibodies induce tolerance while altering interleukin-2,

interleukin-4, tumor necrosis factor, and transforming growth factor-beta production..
AUTHOR: Chavin K D; Qin L; Lin J; Woodward J E; Baliga P; Bromberg J S
CORPORATE SOURCE: Department of Surgery, Medical University of South Carolina, Charleston..
CONTRACT NUMBER: AI31655 (NIAID)
SOURCE: ANNALS OF SURGERY, (1993 Oct) 218 (4) 492-501; discussion 501-.
Journal code: 0372. ISSN: 0003-4932.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals; Cancer Journals
ENTRY MONTH: 9404 1
AB OBJECTIVE: These studies were designed to elucidate the mechanism by which signals delivered by anti-CD2 monoclonal **antibody** (MoAb) interfere with activational signals delivered by anti-CD3 MoAb and induce long-term graft survival and tolerance. SUMMARY BACKGROUND DATA: Anti-CD2. . . anti-CD2 and/or anti-CD3 MoAb intravenously only at the time of initial allografting. Serum from treated animals and culture supernatants from **lymphocytes** stimulated in vitro with anti-CD3 were examined for interleukin (IL)-2, -4, -6, and -10, tumor necrosis factor (TNF), and transforming growth factor-beta (TGF beta). RNA was isolated from **lymphocytes** from treated animals and examined for **receptor** and cytokine gene expression by northern hybridization or reverse transcribed and amplified by the polymerase chain reaction (PCR). RESULTS: Anti-CD2. . . toxicity. Second donor-specific allografts also showed long-term survival. The peak serum TNF concentration (2100 units/mL) was reduced 78% by anti-CD2 **treatment** (456 units/mL). Anti-CD2 inhibited anti-CD3-stimulated proliferation and in vitro production of IL-2 and IL-4, with no alteration of **IL-6**, IL-10, or TNF. Conversely, there was an increase in the immunosuppressive cytokine TGF beta. PCR analysis showed that anti-CD2 reduced. . . IL-2 messenger RNA expression, and by northern analysis, anti-CD2 inhibited anti-CD3-stimulated increases in messenger RNA for the CD2 and CD3 **receptors** themselves. CONCLUSIONS: The combination of anti-CD2 and anti-CD3 MoAbs induced a state of tolerance while decreasing anti-CD3-associated cytokine toxicity. The. . .

L4 ANSWER 18 OF 21 MEDLINE DUPLICATE 17
ACCESSION NUMBER: 94346109 MEDLINE
DOCUMENT NUMBER: 94346109
TITLE: Characterization of unique lymphoid cells derived from murine spleen which constitutively produce interleukin-6.
AUTHOR: O'Neill H C; Ni K
CORPORATE SOURCE: Division of Clinical Sciences, John Curtin School of Medical Research, Australian National University, Canberra, Australia..
SOURCE: IMMUNOLOGY, (1994 Jun) 82 (2) 220-8.
Journal code: G7F. ISSN: 0019-2805.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
ENTRY MONTH: 199411
AB . . . stimulation was used to expand the lymphoid cells remaining in spleen following depletion of CD4+ and CD8+ T cells by **antibody** and complement **treatment**. Cells were cultured in the presence of concanavalin A (Con A), interleukin-2 (IL-2) and syngeneic irradiated

spleen feeder cells. This. . . unique to T, B or myeloid cells. All cell lines represent agranular lymphoblasts and show no evidence of early T-cell **receptor** (TcR) or Ig heavy chain gene rearrangements, suggesting no commitment to T- or B-lymphoid lineage. Despite expression of the NK1.1 marker. . . factor-alpha (TNF-alpha) or granulocyte-macrophage colony-stimulating factor (GM-CSF) in cell supernatants. However, all but one of these cell lines constitutively produce **IL-6**. Each cell line has been shown to induce T-cell proliferation independently in mixed **lymphocyte** reactions, implicating the capacity of these cells to act as antigen-presenting cells. Consistent with this hypothesis is the observation that. . .

L4 ANSWER 19 OF 21 MEDLINE DUPLICATE 18
ACCESSION NUMBER: 91130017 MEDLINE
DOCUMENT NUMBER: 91130017
TITLE: Enhancement of lymphokine-activated T killer cell tumor necrosis factor receptor mRNA transcription, tumor necrosis factor receptor membrane expression, and tumor necrosis factor/lymphotoxin release by IL-1 beta, IL-4, and IL-6 in vitro.
AUTHOR: Bett A J; Gallagher M; Inions E K; Cappuccini F; Yamamoto R S; Granger G A; Watanaga T
CORPORATE SOURCE: Department of Molecular Biology & Biochemistry, University of California Irvine 92717..
SOURCE: JOURNAL OF IMMUNOLOGY, (1990 Mar 1) 144 (5) 1922-6.
Journal code: IPE. ISSN: 0022-1767.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals; Cancer Journals
ENTRY MONTH: 199103
AB Co-culture with IL-2 can induce human T **lymphocytes** to proliferate and become non-specifically restricted, lymphokine-activated killer (LAK) cells in vitro. Our studies were conducted with long term cultured, . . . 2B8. We found that proliferating 7 to 10-day human T-LAK cells express TNFR, by using a 125I-TNF binding assay. Additional **treatment** of these cells with the cytokines IL-1 beta, IL-4, or **IL-6** rapidly up-regulated steady-state TNFR mRNA transcription and doubled TNFR membrane expression. Further studies revealed that these cytokines also increased the release of TNF and lymphotoxin (LT). **Antibody** neutralization studies indicated that IL-1 induces release of both TNF and LT; however, IL-4 and **IL-6** induce primarily LT release. These results further support the concept that these cytokines are involved in the regulation of TNF/LT release, TNFR synthesis, and TNFR membrane expression. It is apparent that cytokines and their membrane **receptors** are involved in the autocrine/paracrine control of T cell proliferation, differentiation, and expression of functional activity after IL-2 stimulation in. . .

L4 ANSWER 20 OF 21 MEDLINE DUPLICATE 19
ACCESSION NUMBER: 92120773 MEDLINE
DOCUMENT NUMBER: 92120773
TITLE: Tissue-specific homing receptor mediates lymphocyte adhesion to cytokine-stimulated lymph node high endothelial venule cells
AUTHOR: Chin Y H; Cai J P; Xu X M
CORPORATE SOURCE: Department of Microbiology and Immunology, University of Miami School of Medicine, Florida 33101..
CONTRACT NUMBER: AI 26340 (NIAID)
SOURCE: IMMUNOLOGY, (1991 Nov) 74 (3) 478-83.
Journal code: ORF. ISSN: 0019-2805.
PUB. COUNTRY: ENGLAND: United Kingdom

Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
ENTRY MONTH: 199204

AB **Lymphocytes** bind to high endothelial venule (HEV) cells as the first step in the migration of these cells into lymph nodes. . . and cultured HEV cells from rat LN and investigated the effects of cytokines on the adhesiveness of these cells for **lymphocytes**. The results showed that **lymphocytes** from thoracic duct, spleen and LN adhered preferentially to the cultured LN HEV cells compared to cells isolated from the thymus and bone marrow. The adhesiveness of LN HEV cells for thoracic duct **lymphocytes** (TDL) was significantly increased in a dose- and time-dependent manner by pretreatment of the HEV cells with tumour necrosis factor-alpha (TNF-alpha), interferon-gamma (IFN-gamma) or interleukin-4 (IL-4). In contrast, pretreatment of HEV cells with IL-1, **IL-6** or IL-7 did not alter the capacity of LN HEV cells to adhere **lymphocytes**. Furthermore, incubation of LN HEV cells with suboptimal doses of TNF and IL-1, IFN-gamma and IL-4, or TNF-alpha and IFN-gamma. . . to increase the adhesiveness. The adhesion of TDL to non-stimulated and IL-4-stimulated LN HEV cells could be blocked specifically by **treatment** of **lymphocytes** with the LN homing-**receptor**-specific A.11.5 monoclonal **antibody** (mAb). In contrast, **lymphocytes** pretreated with the PP-homing **receptor**-specific 1B...6 mAb or the antileucocyte common antigen (OX1) mAb adhered normally to the HEV cells. Taken together, these results indicate that the baseline and cytokine-stimulated bindings between **lymphocytes** and LN HEV cells are mediated by adhesive mechanisms that regulate **lymphocyte** migration into LN in vivo and provide strong evidence that cytokines are central mediators of organ-specific **lymphocyte** migration.

L4 ANSWER 21 OF 21 BIOSIS (COPYRIGHT 200 BIOSIS DUPLICATE 20
ACCESSION NUMBER: 198 9:41869 BIOSIS
DOCUMENT NUMBER: BA88:8 956
TITLE: FUNCTIONAL AND MOLECULAR CHARACTERIZATION OF B CELL LINE DERIVED INTERLEUKIN-1-ALPHA.
AUTHOR(S): VYTH-DREESE F A; HILKMAN A; WIJDENES J; GEERTSMA M; DELLAMAN T R M; DOSDA J; MEIJER C J M; BERTOGLIO J
CORPORATE SOURCE: DEV. IMMUNOL., NETHERLANDS CANCER INST., PLESMANLAAN 121, 1066 CX AMSTERDAM, THE NETHERLANDS.
SOURCE: LEUKEMIA (BALTIMORE), 1989) 3 (8 , 585-592.
CODEN: LEUKEM. ISSN: 0 87-6924.
FILE SEGMENT: BA; CII
LANGUAGE: English

AB. . . supernatant from STS 15 cells (STS 25 SUP) does not show activity in assays for interleukin-2 (IL-2 , -4 (IL-4), -6 (**IL-6**), interferon or tumor necrosis factor, but is active in the thymocyte costimulation assay and the D10.G4.1 T helper clone proliferative. . . The IL-1 character of the STS 25 SUP activity was confirmed in inhibition studies with three different poly-or monoclonal anti-IL-1 **antibodies** (31, 88, and 94% inhibition in thymocyte costimulation assay, respectively). Furthermore, complete blocking of D10.G4.1 cell proliferation mediated by STS 25 SUP was observed by including anti-IL .alpha. specific **antibody** in the assay, whereas anti-IL .beta. **antibody** had no effect. These results indicate that this STS 25 SUP activity can be attributed to the presence of IL-1.alpha . . . constitutive expression of IL- .alpha. messenger RNA by STS 15 cells. In contrast, no IL-1.beta. message was detectable, not even after **treatment** of the cells with phorbol ester or cycloheximide, which resulted in approximately 5-fold enhancement of IL-1.alpha. mRNA

expression. Binding studies with radiolabeled recombinant (r) IL-1.alpha. indicated the presence of high numbers of IL-1 **receptors** on STS 25 cells (1,170 per cell, Kd = 392 pM). Although both IL-1.alpha. and IL-1.beta. bound to these IL-1 **receptors**, no indication was found for IL-1 mediated regulation of STS 25 cell growth. STS 25 SUP as well as rIL-1.alpha. were comparably active in enhancing mitogen stimulated proliferation and/or Ig secretion by normal peripheral blood T **lymphocytes** or normal tonsil B **lymphocytes**. Moreover, STS 25 SUP and rIL-1.alpha., but not recombinant granulocyte/macrophage colony stimulating factor (rGM-CSF), enhanced the proliferation in 1/8 and. . .

=> s (il-6 (a) receptor) (s) antibody (p) lymphocyte (p) treatment

L5 0 (IL-6 (A) RECEPTOR) (S) ANTIBODY (P) LYMPHOCYTE (P) TREATMENT

=> log y

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	45.43	45.64

STN INTERNATIONAL LOGOFF AT 13:28:19 ON 18 DEC 2000